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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,432	01/05/2001	William A. Bachovchin	TUU-P02-006	3173

28120 7590 11/12/2002

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/12/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/601,432	BACHOVCHIN ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 16-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. It is noted that the clean copy of amended claim 29 does not correspond to the marked-up copy of amended claim 29 included in the response filed September 16, 2002. In particular, the phrase "boronyl peptidomimetic" is missing from before "inhibitors" in the clean copy of amended claim 29. The clean copy of the amended claims is the copy that is actually entered into the file wrapper and examined. Accordingly, the claim has been examined without the limitation "boronyl peptidomimetic" being present.

2. The disclosure is objected to because of the following informalities: At page 9, line 6, "organics" is misspelled. Appropriate correction is required.

3. Claims 2-4, 6-14, 16-23, 28, and 31-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-4 are indefinite because they do not explicitly recite what constitutes Formula I. Claims are to complete in and of themselves, and Applicants have not shown that there is no other practical way to define the invention in words, e.g. have not shown that it is not practical to insert the definition of Formula I into the claims. See MPEP 2173.05(s). Note that if claims 2-4 were to be interpreted as being dependent upon claim 1, then issues under 35 U.S.C. 112, second and fourth paragraphs, would be raised because claims 2-4 do not use the standard language of claim dependency, and claims 2-4 recite different methods than does claim 1. At claim 16, lines 12-14; claim 28, page 17 of the amendment filed September 16, 2002, lines 2-3; and claim 31, page 19, lines 10-11; the "including" phrases are indefinite because it is not clear if the scope of the claims is to be limited to the exemplified and/or particularly exemplified substituents or not. It is suggested that the "including" phrases could be deleted and made the subject matter of further dependent claims. The general formula

in claim 28 appears to be incorrect given the definition of R_1 set forth in the claim. The definition of R_1 indicates that, e.g., C-terminally-linked amino acid residues and amino protecting groups are permitted. However, as shown in the general formula, R_1 is not bonded to an amino group. Claim 31 is indefinite because it depends upon itself. The examiner assumes that Applicants intended for it to depend upon claim 30. Claim 31 is indefinite because it defines variables R_5 and R_{61} which are not used in any of the chemical structures found in the claim. The variable R'_7 at claim 31, page 18, line 21, is not defined in the claim. The variable R_{62} at claim 31, page 18, line 3, is not defined in the claim. At claim 37, line 3, "and" should be changed to "or" so that it is clear that all three dipeptides do not have to be mimicked simultaneously.

4. Claims 1-14, 16-26, 28, and 30-36 are objected to because of the following informalities: At claim 1, page 6 of the amendment filed September 16, 2002, lines 7 and 10, the underlining should be removed from the claim. At claim 1, page 6, line 10, "or" should be deleted. Claim 9 does not end with a period. At claim 24, page 11, line 9; claim 25, page 12, line 9; claim 26, page 13, line 10; claim 28, page 16, line 4; and claim 31, page 19, line 7; "or" should be inserted before the last chemical structure in the line. At claim 24, page 11, line 12, "a" (first occurrence) should be changed to "an". At claim 28, page 17, line 8, a semicolon should be inserted at the end of the line. At claim 30, line 2, "a" should be inserted after "including". At claim 32, line 3, a conjunction, e.g., "or" or "and", should be inserted before "hyperlipoproteinemia". Appropriate correction is required.

5. Claim 26 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The definition of X_1 in claim 26 indicating that the substituent can be hydrogen is not embraced by the definition of X_1 in claim 16.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14 and 16-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-67 of copending Application No. 09/628,225. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '225 application anticipate the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. The effective filing date of instant claims 1-14 and 16-37 is deemed to be February 2, 1998, the filing date of provisional application 60/073,409. Instant claims 1-14 and 16-37 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of the parent provisional application because the parent provisional application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed invention. Accordingly, the Deacon et al article

(Diabetes, Vol. 47, pages 764-769) and the WO Patent Application 98/25644 are not available as prior art against these claims. (Drucker, U.S. Patent No. 5,952,301, in the same patent family as the WO Patent Application '644, is not applied against the instant claims because Drucker does not contain any disclosure concerning the use of dipeptidylpeptidase inhibitors.)

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 1-3, 5-13, 16, 20, 21, 25, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '309. The WO Patent Application '309 teaches administering DPIV inhibitors to treat human disease. The inhibitors are highly potent, with Ki values ranging into the nanomolar range or less, and are chemically stable. The DPIV inhibitors with the smallest Ki have the same structure as is set forth in Applicants' claims 15, 16, 20, 21, and 25. See, e.g., page 3, lines 10-21; page 4, lines 1-3; compounds 23, 38-40 and 97; and Table 9. Because the same active agents are being administered to the same animals according to the same method steps, inherently metabolism of GLP-1, glucose metabolism, insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, hyperlipoproteinemia, and peptide hormone metabolism will be modified to the same extent in the method of the WO Patent Application '309 as is claimed by Applicants. With respect to instant claims 8-10, in view of the similarity in structure and function between the DPIV inhibitor of the WO Patent Application '309 and Applicants' claimed DPIV inhibitor, the EC50's and Ki for the DPIV inhibitor of the WO Patent Application '309 will inherently be the same as is recited in instant claims 8-10. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitor of the WO Patent Application '309 and the inhibitors recited in

Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of the WO Patent Application '309.

10. Claims 1-3, 5-13, 16-24, 26, 27, 29-35, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '259. The WO Patent Application '259 teaches inhibiting the enzymatic activity of DPIV in a mammal by administering a peptide compound. The peptides compounds are proteolyzed by DPIV in vivo until a C-terminal dipeptide portion remains, which acts as an inhibitor of DPIV. The peptide compound is more stable in vivo than the C-terminal dipeptide portion. If the C-terminal dipeptide portion is chosen to be a dipeptide prolyl-boronic acid, then a potent and highly specific inhibitor having a Ki in the nanomolar range is ultimately released in vivo. Tetrapeptides comprising Ala-boroPro and Pro-boroPro as the C-terminal dipeptide portions are taught. As an alternative to the boroPro group, trifluoroalkyl ketone groups are taught. See, e.g., page 2, lines 15-32; page 3, line 1 - page 7, line 16; page 14, lines 10-12; and page 14, line 34 - page 15, line 16. Because the same active agents are being administered to the same animals according to the same method steps, inherently metabolism of GLP-1, glucose metabolism, insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, hyperlipoproteinemia, and peptide hormone metabolism will be modified to the same extent in the method of the WO Patent Application '259 as is claimed by Applicants. With respect to instant claims 8-11 and 33-35, in view of the similarity in structure and function between the DPIV inhibitors of the WO Patent Application '259 and Applicants' claimed DPIV inhibitors, the EC50's and Ki's for the DPIV inhibitors of the WO Patent Application '259 will inherently be the same as is recited in instant claims 8-11 and 33-35. Sufficient evidence of similarity is deemed to be present between the

DPIV inhibitors of the WO Patent Application '259 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of the WO Patent Application '259.

11. Claims 1-14 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Villhauer. Villhauer teaches treating non-insulin-dependent diabetes, i.e. Type II diabetes, and increasing glucose tolerance by administering a DPIV inhibitor having the same structure as Applicants' claim 1. The inhibitors improve early insulin response to oral glucose challenges. Oral administration of the inhibitors is taught. See, e.g., the Abstract; column 9, lines 48-65; and column 10, lines 28-42. With respect to instant claims 2 and 8-11, in view of the similarity in structure and function between the DPIV inhibitor of Villhauer and Applicants' claimed DPIV inhibitor, the EC50's and Ki for the DPIV inhibitors of Villhauer will inherently be the same as is recited in instant claims 2 and 8-11. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitors of Villhauer and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of Villhauer. With respect to instant claim 29, because the same active agents are being administered to the same animals according to the same method steps, inherently peptide hormone metabolism will be modified to the same extent in the method of Villhauer as is claimed by Applicants.

12. Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by the German Patent 196 16 486. The German Patent '486 teaches using DP IV inhibitors to inhibit degradation of gastric inhibitory peptides and glucagon-like peptides, which effect can be used to reduce blood sugar levels and to treat diabetes mellitus. Inhibitors include alanyl pyrolidide, isoleucyl

thiazolidide, and N-valyl prolyl, O-benzoyl hydroxyl amine, and they can be administered orally. See, e.g., pages 1-2; page 10, line 21 - page 11, line 1; and page 11, line 15; of the attached translation. In view of the similarity in structure and function between the DPIV inhibitors of the German Patent '486 and Applicants' claimed DP IV inhibitors, the EC_{50} and K_i values for the DP IV inhibitors of the German Patent '486 will inherently be the same as those recited in the instant claims. Sufficient evidence of similarity is deemed to be present between the DP IV inhibitors of the German Patent '486 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than those of the German Patent '486.

13. Applicant's arguments filed September 16, 2002 have been fully considered but they are not persuasive.

Numerous objections and rejections of the specification and claims set forth in paragraphs 4-7 of the first Office action have been carried over into this Office action because, although Applicants state in their Remarks that amendments were made to overcome the objections and rejections, no such amendments were found in Applicants' response by the examiner. Any proposed corrections to the chemical formula recited in claim 28 will at least require reconsideration of the prior art of record to determine whether compounds having the corrected formula have been taught to be administered in vivo. This could raise issues, e.g., of inherency, analogous to those already present in the application. Also, concerning Applicants' response at page 41, section 8, the examiner could not find any correction with respect to the subject matter originally appearing at claim 15, page 54, line 15.

Concerning Applicants' statement at page 42, line 10, of the response, Applicants clearly have not canceled claims 1-29.

The anticipation rejections based upon the WO Patent Application 95/15309 and the WO Patent Application 93/08259 are maintained. Applicants' argument that accidental unwitting achievement of a claimed result can not constitute anticipation is not accepted because by definition, the doctrine of inherency requires the accidental or unwitting achievement of Applicants' claimed result. Applicants' analysis would mean that inherency rejections could never be made, a result which is not supported by the case law. Applicants' citation to Marshall is noted; however, Marshall does not represent the current state of the case law with respect to inherency and anticipation rejections. See MPEP 2112 and 2112.02 and especially Ex parte Novitski, 26 USPQ2d 1389, 1391 (BPAI 1993) cited therein. See also W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1548, 220 USPQ 303, 309(Fed. Cir. 1983) (holding that it is irrelevant to the determination of anticipation whether those using the invention appreciated the results because "[w]ere that alone enough to prevent anticipation, it would be possible to obtain a patent for an old and unchanged process"), cert. denied, 469 U.S. 851 (1984) and Abbott Labs. v. Geneva Pharms., Inc., 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1309(Fed. Cir. 1999) (stating that the "accidental and unwitting" cases are only applicable when the claimed invention is "anticipated by earlier work that produced no useful or appreciated result"), cert. denied, 528 U.S. 1078 (2000).

The rejection based upon Villhauer is maintained. Claims 1-4 still define W as embracing "a functional group which reacts with an active site residue of the targeted protease", which language encompasses the cyano group of Villhauer.

The rejection of claim 29 over the German Patent '486 is maintained as claim 29 hasn't yet been amended to require boronyl peptidomimetic inhibitors of dipeptidyl peptidase IV.

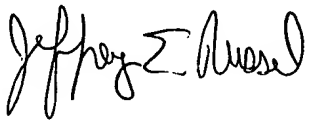
14. Claim 36 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. The prior art of record does not teach the oral administration of boronyl peptidomimetics having the structure recited in instant claim 31, and does not teach or suggest that such oral administration would result in modifying glucose metabolism of an animal.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

November 7, 2002